UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,974	01/27/2000	Connie S. Schmaljohn	003/115/SAP RIID96-10	9304

7590 04/08/2004

Attn MCMR JA Elizabeth Arwine Patent Atty
U S Army MRMC
504 Scott Street
Fort Detrick, MD 21702-5012

EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/491,974	SCHMALJOHN ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 January 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *December 23, 2003* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed January 27, 2000, claims benefit of provisional application 60/117,680, filed January 29, 1999.

Applicants' amendment filed January 21, 2004, has been received and entered. Claims 28, 37, 48 and 49 have been amended. Claims 28-51 are pending and currently under examination.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-43 of copending Application No. 10/394,388 (2004/0053216 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the same compositions and same methods. It is noted that 10/394, 388 is indicated to be a continuation in part of 09/941,974, however this appears to be an error, and that the correct claim should be made to the instant application. A review of the polynucleotide sequences in both

disclosures indicates that they are the same. The differences between the two disclosures appears to be only in the working examples provided in '388. The working examples appear to provide similar information as that provided in the declaration provided during the prosecution of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Amendment

The declaration of Jay Hooper filed under 37 CFR 1.132 filed June 30, 2003, paper number 24, is insufficient to overcome the rejection of claims 28-32, 35-41, 44, 45, 48 and 49 based upon 35 USC 103 as set forth in the last Office action because: it is unclear from the data presented in the declaration that demonstrates the unexpected results of administering and expressing both G1 and G2 glycoprotein of a hantavirus M gene is commensurate in scope with the instant claims. More specifically, claim 28 encompasses a composition comprising (a) an inert particle coated with a polynucleotide, and (b) the polynucleotide on said particle wherein said polynucleotide comprises a promoter operatively linked to a hantavirus M gene encoding both a G1 glycoprotein and G2 glycoprotein, however from the experiments detailed in the declaration, it is not clear how the immunization was done or if the immunization was done with the instantly claimed composition. Examiner would agree that the results presented in the declaration clearly indicate that administration and expression of both G1 and G2 glycoproteins of a hantavirus M gene are required to provide protective immunity to hantavirus. Furthermore, Examiner would note that the experiments demonstrate that the protective immunity provided by

the expression of both G1 and G2 glycoproteins of one specific hantavirus M gene extends protective immunity beyond the one specific hantavirus represented by the G1 and G2 glycoprotein sequences of the hantavirus M gene expressed as exemplified in Table 2 of the declaration (page 3 of declaration). However, while the details of the experiments indicate that expression of both G1 and G2 glycoproteins of a hantavirus M gene have the unexpected result of providing protective immunity, the results do to clearly indicate that this unexpected result extends to compositions wherein the polynucleotide is coated onto inert particles for administration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-51 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schmaljohn (Rev. Med. Virol., 4:185-196, 1994), Chu *et al.* (J. Virol., 69(10):6417-6423, 10/95), Montgomery *et al.* (Pharmacol. Ther., 74(2):195-205, 1997), Donnelly *et al.* (Ann. Rev. Immunol., 15:617-648, 1997), and Arikawa *et al.* (Virol., 176:114-125, 1990).

Applicants note the amendments to the claims and argue that the none of the five references provide the necessary guidance to express both G1 and G2 to affect a protective immunity when administered to a mammal (see Applicants' amendment page 8). In addition,

Applicants note the Examiner's reasons for not finding the declaration convincing and indicate that the experiments performed as evidence in the declaration were performed with polynucleotides coated onto gold beads and administered with a gene gun (see Applicants' amendment, page 9). Applicants arguments have been fully considered, but not found persuasive.

Initially, Attorneys comments regarding the details of the experiments performed in the declaration are noted, however the arguments of counsel cannot take the place of evidence in the record . *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716,718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results. MPEP 716.01(c). Moreover, given the limited number of sequences and details provided in the declaration it is unclear if this unexpected result would extend beyond the specific vectors and sequences used. The claims are broad encompassing the use of any Hantaan virus G1-G2 or M sequence, and it is unclear if the immunity provided in using SEQ ID NO: 1 or 3 would extend to sequences from other virus. With respect to using both G1 and G2, it is noted that Schmaljohn teaches to use the entire M region which comprises and encodes G1 and G2. Further, it taught the G1 and G2 are the major proteins involved in the induction of immunity. Clearly, Schmaljohn provide the necessary teaching that both G1 and G2 are important and provide examples where both comprised in the M region are expressed from a recombinant vector to affect immunity in a subject. Applicants arguments that the references do not teach to provide both G1 and G2 are not found convincing because Schmaljohn teaches the importance of both these proteins in protective immunity and provides vectors for the expression of both.

For the reasons above and of record, the rejection is maintained.

Claims 28-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmaljohn *et al.* (US Patent 5,614,193), Schmaljohn (Rev. Med. Virol., 4:185-196, 1994), Chu *et al.* (J. Virol., 69(10):6417-6423, 10/95), Montgomery *et al.* (Pharmacol. Ther., 74(2):195-205, 1997), Donnelly *et al.* (Ann. Rev. Immunol., 15:617-648, 1997), and Arikawa *et al.* (Virol., 176:114-125, 1990).

Schmaljohn reviews prospects for vaccines to control hantavirus infections. Schmaljohn summarizes the state of the art concerning mechanisms of immunity to hantaviral inventions and discloses that the envelope glycoproteins, G1 and G2 are presumed to be the major elements involved in induction of immunity to hantaan virus (e.g. p. 187, left col.). Schmaljohn further reviews the results of analyses involving recombinant vaccinia virus- or baculovirus-vector candidate vaccines, expressing the entire M segment, portions of the M segment encoding only G1 or only G2, the S segment, or both the M and S segments of HTN virus strain 76-118 wherein 9/9 hamsters immunized once and 4/4 immunized twice with baculovirus recombinants expressing the complete M segment (both the G1 and G2 proteins) were protected from challenge. In contrast, incomplete protection was observed using vaccinia recombinants expressing only G1 or only G2 and no protection was observed using vaccinia/S segment recombinants. Schmaljohn does not disclose the specific sequences used in the examples nor polynucleotide compositions coated onto carrier particles or methods of their use as a vaccine.

Schmaljohn *et al.* (US Patent 5,614,193) teach at the time of filing that the hantaan virus sequences encoding G1 and G2 disclosed in the instant application were known. Further, the

sequences were used as vaccines in recombinant vectors which expressed the proteins when delivered to a subject. Further, Chu et al. teach generally that a vaccinia virus-vectored vaccine expressing the M and S segments of Hantaan (HTN) virus could elicit a protective immune response against other hantaviruses, including other Hantaan and Seoul viruses.

Montgomery *et al.* reviews the state of the DNA vaccine art and teaches that "[i]f known antigens elicit protective antibodies from a natural infection, results in many disease models support the hypothesis that expression of the antigen from a plasmid will elicit a similar response" (p. 198, left col.). Montgomery further teaches that gene gun delivery of plasmid DNA by adsorption to gold particles offer a convenient and highly sensitive method for achieving humoral and cellular immune responses with as little as 16 ng plasmid in rodent animals (p. 200, left col.).

Donnelly et al. reviews the state of the DNA vaccine art and teaches DNA vaccines offer a simple alternative to other methods involving e.g. live attenuated vaccinia virus recombinants which "may be restricted in use due to concerns about their safety" (p. 619). Donnelly further draw attention to the "remarkable number of publications demonstrating efficacy of DNA vaccines in various preclinical models that have appeared since the publication of the initial demonstration of the generation of protective efficacy attest to the simplicity as well as the robustness of the technology" (p. 620) and discusses the advantage and simplicity associated with being able to alter constructs or mixing different plasmids to explore the use of e.g. different forms of an antigen or effects of coexpressed cytokines, as well potentially broader, simultaneous protection against different strains and/or antigens by utilizing a combination or "cocktail" DNA vaccine consisting of multiple discrete plasmids encoding several different

pathogen antigens or combinations of pathogens to induce a broader spectrum of immune responses from a single preparation (see e.g. p. 625). Donnelly further teaches the benefits of gene gun-mediated DNA vaccine transfer as exemplified by studies comparing the induction of CTL using an influenza NP construct administered epidermally by the gene gun or intradermally by needle injection indicat[ing] that, for this particular construct, injection of 1 μg of DNA i.d. with a conventional needle did not induce CTL whereas as little as 16 ng of DNA did induce CTL by gene gun immunization" (p. 627).

Arikawa et al. discloses the coding properties of the M and S genome segments of the Sapporo rat (SR-11) hantavirus, the etiologic agent of mehorrhagic fever with renal syndrome (HFRS), whose protein coding regions comprise those matching SEQ ID NOs:1 and 2 of the instant application. Arikawa teach that their SR-11 M and S genome segment studies should "provide a basis for the thoughtful development of hantavirus recombinant DNA vaccines and diagnostic reagents" (p. 124, left col.).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to redevelop the vaccinia virus/hantavirus candidate vaccines of Schmaljohn and Chu comprising M and S genome segments by incorporating the teachings of the DNA vaccine art, since Montgomery teaches that a knowledge of antigens found to be important in protective immunity can be incorporated in the design of DNA vaccines, based on "results in many disease models [which] support the hypothesis that expression of the antigen from a plasmid will elicit a similar response". One of ordinary skill in the art would have been further motivated to combine these teachings in view of the advantages of DNA vaccines over live vaccinia virus vaccines since DNA vaccines are predicted to be safer, easier to maintain, less expensive, and offering

greater flexibility, including protection against multiple antigens and/or pathogens as suggested by Donnelly. It would have been obvious to design plasmid vectors encoding M and/or S genome segments coated onto gold carrier particles for gene gun-mediated delivery into the epidermal cells of a mammal, since Montgomery and Donnelly teach the dramatic effects of using small amounts of DNA (cheaper) for gene-gun-mediated delivery into epidermal cells. Design of such vectors, including those comprising the M and S genome segments of SR-11 as suggested by Arikawa in accordance with the cross-protection results of Chu, would have been predicted, with a reasonably high expectation of success, based on the suggestions of Montgomery and Donnelly to have resulted in cheaper, more convenient and potentially more effective vaccines compared to those of Schmaljohn and Chu.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
AU1632